#12 Ex (4) of Amend D

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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SERIAL NO.: 09/762,643 GROUP: 1655

FILED: JANUARY 31, 2002

FOR: VESSEL FOR WITHDRAWING BLOOD

AMENDMENT AFTER FIRST OFFICE ACTION

BOX NON-FEE AMENDMENT
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Office letter of January 31, 2002, please amend the above-identified application as follows:

IN THE CLAIMS:

Amend claims 1 and 3 to read as follows:--

1 (amended). A blood withdrawing vessel containing a nucleic acid-stabilizing aqueous solution for stabilizing nucleic acids in the withdrawn blood directly upon contact with the solution, the solution comprising the following components:

- a guanidinium salt in a concentration of 1 to 8.0 M;
- a buffer substance in a concentration of 10 to 300 mM;
- a reducing agent in a concentration of 5 to 30%, by wt; and
- a detergent in a concentration of 0.1 to 10%, by wt.

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3 (twice amended). The vessel according to claim 1, characterized in that the guanidinium salt is present in a concentration of 2.5 to 8.0 M.

D2

Cancel claims 5, 7 and 9.

Amend claim 10 to read as follows: --

10 (twice amended). The vessel according to claim 1, characterized in that the pH of the solution is between 4.0 and 7.5. --

D3

Add the following claim after amended claim 10:--

25. The vessel according to claim 10, characterized in that the pH of the solution is between 4.0 and 6.5.--

D4

Amend claims 14 and 16 to read as follows: --

14 (twice amended). A method of withdrawing blood, comprising the step of directly introducing the blood into a vessel according to claim 1.

D5

16 (amended). The method according to claim 15, characterized in that the concentration of the guanidinium salt after the blood is introduced is between 1.0 M and 5 M. --

Add the following claim after amended claim 16:--

26. The method according to claim 16, characterized in that the concentration of the guanidinium salt, after the blood is introduced, is between 1.5 and 5 M. --

Amend claim 18 to read as follows: --

18 (amended). The method according to claim 14, characterized in that the pH of the solution is adjusted such that, following the introduction of the blood, a pH between 4.0 and 7.5 is obtained. --

Cancel claims 19 and 20.

Amend claim 22 to read as follows: --

22 (twice amended). The blood sample according to claim 24, characterized in that it has a pH of 4.0 to 7.5. --

Add the following claim after amended claim 22:--

27. The blood sample according to claim 22, characterized in that it has a pH of 6.6 to 7.0.--

D10

Amend claim 24 to read as follows: --

24 (amended). A stabilized blood sample containing a reaction product of blood and the aqueous solution of claim 1. --

D11

REMARKS

The claims have been amended in an effort to overcome the rejection under 35 U.S.C. 112. The claims rejected under 35 U.S.C. 102 have ben canceled, and the preferred features have been set forth in separate claims. Also, claim 1 now explicitly sets forth the subject matter described in the first full paragraph on page 4, i.e. that the aqueous solution in the blood withdrawing vessel is a nucleic acid-stabilizing solution for stabilizing nucleic acids in the withdrawn blood directly upon contact with the solution. The claim also sets forth the concentration of the components, recited in claims 3, 5 and 7.

If applied to the amended claims, the rejection of the claims under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over the cited Hargraves patent is respectfully traversed.

The claims are directed to a "blood withdrawing vessel" and, more particularly, to such a vessel "containing a nucleic acid-stabilizing aqueous solution for stabilizing nucleic acids in the withdrawn blood directly upon contact with the solution." In a long line of appellate decisions, the courts have given patentable weight to the introductory words or preamble of a claim. In a painstaking and exhaustive analysis

of some 37 prior decisions, the Court of Customs and Patent Appeals way back in 1951 determined in **Kropa v. Robie and Mahlman**, 88 USPQ 478, that

> "where the preamble to the claims was expressly or by necessary implication given the effect of a limitation, the introductory phrase was deeemed essential to point out the invention defined by the claim...the preamble was considered necessary to give life, meaning, and vitality to the claims...there inhered in the article specified in the preamble a problem which transcended that before prior artisans and the solution of which was not conceived by or known to them."

And confirming this line of thinking in a recent decision, the Court of Appeals, Federal Circuit, held in **Rowe v. Dror**, 42 USPQ 2d 1550, at 1552,

> "This appeal depends on whether the claim phrase 'balloon **angioplasty** (court's emphasis) catheter,' which appears only in the claim preamble, is or is not an affirmative limitation of the claim. The Board interpreted the claim as 'drawn to the subject matter of a balloon catheter of general utility. amd gave no meaning to the word 'angioplasty.'... Inspection of the entire record in this case reveals that 'angioplasty' is, in fact, a structural limitation of Rowe's claims."

It is respectfully submitted that "inspection of the entire record (i.e. applicant's specification) reveals" that it is the sole object of the claimed invention to stabilize nucleic acids in withdrawn blood immediately and before they are decomposed by other components of biological cells, such as

nucleases, (i.e. "directly upon contact") so that they are protected and available for later assays of the withdrawn blood. Thus, just as a balloon **angioplasty** catheter patentably distinguished over a balloon catheter of general utility in the **Rowe** case, applicant's **blood withdrawing** vessel, in and by itself, patentably distinguishes over Hargreaves' assay vessel, used to determine the presence of a variety of substances encountered in biologicval fluids, such as proteins, drugs, hormones, vitamins, microorganisms, etc. (col. 1, lines 32-36).

Hargreaves' assay vessel is specifically prepared to arrange the reagents in the vessel in layers (see columns 9 and 10) so as to prevent a premature mixing, which would make the vessel useless for this purpose. Quoting **Kropa**, "there inhered in the article specified in the preamble (a blood withdrawing vessel containing a nucleic acid-stabilizing aqueous solution for stabilizing nucleic acids in teh withdrawn blood directly upon contact with the solution) a problem which transcended that before prior artisans (Hargreaves) and the solution of which was not conceived by or known to them."

It is true that Hargreaves mentions a guanidinium salt (col. 17, line 23), a buffer susbtance (col. 5, line 21), a reducing agent (col. 31, line 9), as well as a detergent (col. 12, line 9) among his large number of reagents. However, it is

respectfully submitted that, at the time the present invention was made (Sec. 103), it was **not** obvious to a person of ordinary skill in the art to select four specific compounds from the vast number of reagents used by Hargreaves for a vast number of different assays to stabilize nucleic acids in withdrawn blood on contact. As his claims clearly show, Hargreaves is **not** concerned with any specific components but with the **structure**, i.e. their layering. His patent deals exclusively with the final analysis of a sample, for instance blood **after** it has been drawn, and **not** with stabilizing a component in the sample, i.e. nucleic acids in blood **as** it is drawn. The only example of blood as a sample to be analyzed is Example XIII. In this case, glycosylated hemoglobin is introduced in the assay vessel in a dilution of 1:10. As is known, glycolysated hemoglobin has been subjected to various preparations, i.e. it is not blood as it is being withdrawn.

In contrast to Hargreaves' teaching, which would apply to blood **analysis**, applicant deals with a specific preparation of blood as it is withdrawn so that the nucleic acids in the blood are stabilized and are present in the **subsequent** analysis of the blood. Hargreaves teaches nothing in this respect, and certainly does not suggest the **specific selection** of components to solve a problem never encountered by Hargreaves. Therefore,

this specific combination of components to solve a specific problem is respectfully submitted to add additional weight to the patentability of the blood withdrawing vessel set forth in the preamble. Hargreaves is not concerned with the subject matter of the claimed invention, as set forth in the preamble, i.e. he deals with non-analogous art. He deals with the **analysis** of biological substances. Applicant deals with the **stabilization** of a component in such substances. Neither the subject matter of the preamble nor of the body of claim 1 is obvious from the cited patent. The dependent claims all are directed to specific features, none of which is suggested by Hargreaves in the setting of claim 1. Each one of these combination is, therefore, believed to be patentable on its own merit.

Acknowledgement of the priority claim under 35 U.S.C. 119 is respectfully solicited.

A sincere effort having been made to overcome all grounds of rejection, favorable reconsideration and allowance of claims 1-4, 6, 8, 10-18 and 22-27 are respectfully solicited.

Respectfully submitted,

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Enclosure: Marked-up copy of changes

I hereby certify that this correspondence is being sent by telefax to the US PTO, fax number 703-872-9306 on April 25, 2002.

Ingrid Mittendorf

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